Letters to the Editor

Oral contraceptives and diabetes mellitus: an update

There has long been interest in the possible relationship between oral contraceptive (OC) use and diabetes mellitus. In 1991, we reported our findings (in this Journal) on 45 women who had been referred to hospital for diabetes during follow-up in the Oxford-Family Planning Association (Oxford-FPA) contraceptive study. No association was found with OC use.[1] We nonetheless thought it would be of interest to comment briefly on the findings for this disease up to the time that individual follow-up of the study participants ceased in July 1994 (follow-up of cancer registrations and death notifications is still continuing).

The Oxford-FPA study methods have been described in detail elsewhere.[2] In brief, the study includes 17 032 white women who, when recruited between 1968 and 1974, were married and aged between 25 and 39 years. At entry, 56% were using OCs, 25% a diaphragm and 19% an intrauterine device. These women (save for certain subgroups – see Vessey and Painter[3]) were followed up annually and information was collected about changes in contraceptive methods, pregnancies and their outcome, hospital referrals and deaths. Women who at entry to the study reported that they were suffering from diabetes were excluded from the present analyses. There were 81 cases remaining. Only the first hospital referral (inpatient or outpatient) was taken into account in the analyses.

As expected, hospital referral was strongly positively related to age and body mass index (BMI). In addition, referral was three times as common in women of lower social class (IV–VI) as in women of upper social class (I–II), a difference only partly explained by BMI. Analyses of hospital referral rates in relation to OC use were therefore adjusted for age, BMI and social class.

Our first analysis compared women ever using OCs with those never doing so. The rate ratio was **0.8** with a 95% confidence interval (CI) ranging from 0.5 to 1.3. Rate ratios for hospital referral in relation to total duration of OC use were as follows (95% CIs are given in parentheses): *never used*, **1.0** (reference category); *1–48 months*, **0.9** (0.3–2.1); *49–96 months*, **0.7** (0.3–1.7); *97–144 months*, **0.9** (0.5–1.7); *145 months or more*, **0.6** (0.2–1.6). Corresponding rate ratios in relation to interval since last use of OCs were as follows: *never used*, **1.0** (reference category); *current–48 months*, **0.7** (0.3–1.4); *49–96 months*, **0.7** (0.3–1.7); *97–144 months*, **0.6** (0.2–1.5); *145 months or more*, **1.5** (0.7–2.8). The data were too few to enable analyses to be done by type of OC, but it should be noted that preparations containing 50 μg oestrogen made up 67% of OC exposure. OCs containing a greater amount of oestrogen provided only 2% of exposure.

We recognise the shortcomings of our data, which include the small number of affected women and the associated fact that only those referred to hospital with diabetes were identified. Nonetheless we believe that our case finding has been unbiased with respect to OC use. Furthermore, as we have pointed out previously,[1] if such a bias existed it might be expected to lead to hospital referral of more OC users than non-users.

In conclusion, the final results of the Oxford-FPA study with respect to diabetes mellitus offer further support to the view that OC use does not increase the risk of clinical diabetes mellitus, a finding in keeping with most other studies.[4–6]

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Increase in IUD expulsions

We write to raise awareness of an apparent increase in intrauterine device (IUD) expulsions noted since we started using the TT380 Slimline® in Autumn 2005.

As clinic policy we changed our preferred first-choice copper IUD to TT380 Slimline, mainly because of its 10-year licence compared to 8 years with the T-Safe® Cu380A. In early 2006 we noticed that a number of women were returning soon after insertion with either full or partial expulsion.

Two experienced doctors fit the majority of IUDs, either personally or as part of supervision for the FFPRHC Letter of Competence in Intrauterine Techniques (LoC IUT). We reviewed their IUD data from 1 January 2005 to 1 March 2006, choosing the dates to give roughly equivalent numbers of T-Safe Cu380A and TT380 Slimline insertions. We excluded insertions done by any other clinicians.

From the computer database we were able to identify those women who had not returned for follow-up and those who did not continue with the IUD. Only expulsions occurring in the first 3 months after insertion were included, although later expulsions also appear to be increased. We also noted an increase in women asking to have their IUD removed within the first 3 months. The results are shown in Table 1.

Table 1 *Summary of IUD fitting data*

Device	Total fittings (*n*)	No data (*n*)	No follow-up (*n*)	Expelled (refits) (*n*)
T-Safe® Cu380A	115	3	24	0
TT380 Slimline®	108	1	19	7 (4)
Nova-T® 380	15	1	2	0
GyneFix®	8		3	0
Mirena® (IUS)	196	2	39	2 (1)

IUS, intrauterine system.

Of the seven women who expelled the TT380 Slimline, four also expelled a replacement device. Similarly, of the two women who expelled the intrauterine system, one was known to have a fibroid uterus and also expelled her replacement device. None of the expelled devices had been fitted as part of LoC IUT training.

Although this is only a small observational study, we are concerned that this may be early evidence of a problem with the design of the TT380 Slimline. The plastic frame of this device seems to be softer and less springy than the T-Safe Cu380A and the discontinued, but similar, Ortho Gynae T380®. The TT380 Slimline takes longer to open fully post-fitting *in vitro*. We are careful to fit the device immediately after loading so the device is compressed within the tube for as little time as possible.

We value feedback from colleagues on their experience of using the TT380 Slimline.

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Liquid-based cytology

We very much welcome Dr Williams' commentary[1] in the July 2006 issue of the Journal on any advantage that liquid-based cytology (LBC) may offer and his critical analysis of the systematic review by Davey *et al*.[2] It is surprising that the favourable results of the large five pilots on LBC of England, Scotland and Wales were not included. Two recent publications from this country echo the LBC pilots as regards significant reductions in inadequate rates with LBC.[3,4]

Our positive experience at PathLinks with LBC are in line with these publications. PathLinks is a pathology network, which serves Greater Lincolnshire and Goole; the catchment population is approximately one million. The laboratory processes around 65 000 cervical cytology samples annually. PathLinks cytology service implementation of LBC began in June 2005, with one of the six PCTs converting every 6 weeks coinciding with training completion of a pathologist, a checker and three cytoscreeners. A total of 30 staff converted and provide the present service. Turnaround time just prior to conversion was 6 weeks. Presently this is 2 weeks, with around 90% of results being reported within a week. The inadequate rates were as follows: pre-conversion (April 2004–March 2005) 7.75%, during conversion (April 2005–March 2006) 4.9% and post-conversion 0.8%. The high-grade rates during these periods were 0.89%, 0.95% and 1.1%, respectively, suggesting concordance with the expectation of increased sensitivity of LBC. Our cytoscreeners have found the LBC slides to be 'clean' and easier to study as compared to conventional smears. Detection of endometrial cells is more frequent although this often causes diagnostic difficulty. Our cytoscreeners would be reluctant to return to interpreting conventional smears.

Whether the LBC can be made more cytoscreener-friendly is being explored by the NHS Health Technology Assessment Programme through the MAVARIC trial. Automated technology may make identification of abnormal cells easier. The computerised software will direct the cytoscreeners to probe some 20 locations on a slide rather than painstakingly scanning the whole slide. Furthermore, one of the machines (FocalPoint™) can sort the abnormal slides into quintiles. Up to 25% of the samples are likely to be classified as 'no further review' meaning that manual reading is not required. The MAVARIC trial set up in August 2005 compares two automated cervical screening technologies with manual screening. Cytology samples are randomly allocated to reading by manual screening alone or by one of the two automated technologies backed up by manual screening. The trial is expected to end in 2009 and the published results are due in 2011. Further uses of LBC are being actively researched. LBC lends itself to the hybrid capture technique for the human papillomavirus test[5] and for chlamydia screening.[6]